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## Validation of static and dynamic radiostereometric analysis of the knee joint using bone-models from CT data

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# Title page

## **Validation of static and dynamic radiostereometric analysis of the knee joint using bone-models from CT data.**

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## ABSTRACT

Objectives: Static radiostereographic analysis (RSA) using implanted markers are considered the most accurate system for the evaluation of prosthesis migration. By using computed tomography bone-models instead of markers combined with a dynamic RSA system, a non-invasive measurement of joint motion is enabled. This method is more accurate than current 3D skin marker-based tracking systems. The purpose of this study was to evaluate the accuracy of the CT model-method for measuring knee joint kinematics in static and dynamic RSA using the marker-method as the gold standard.

Methods: Bone-models were created from CT scans, and tantalum beads were implanted into the tibia and femur of eight human donor knees. Each specimen was secured in a fixture, static and dynamic stereo radiographs were recorded, and the bone-models and the marker-models were fitted to the stereo radiographs.

Results: Results showed a mean difference between the two methods in all six degrees of freedom (6DOF) for static RSA to be within  $-0.10$  to  $0.08$  mm/ $^{\circ}$  with a 95% Limit of Agreement (LoA) ranging from  $\pm 0.49 - 1.26$ . Dynamic RSA had a slightly larger range in mean difference of  $-0.23 - 0.16$  mm/ $^{\circ}$  with LoA ranging from  $\pm 0.75 - 1.50$ .

Conclusions: In a laboratory controlled setting, the CT model method combined with dynamic RSA may be an alternative to prior marker-based methods for kinematic analyses.

## KEYWORDS:

Radiostereographic analysis, Dynamic, CT bone-model

**Article focus:**

- Validation of the accuracy of a model-method using CT bone-models for measuring knee joint kinematics in static and dynamic radiostereometric analysis using the marker-method as the gold standard.

**Key messages:**

- We believe the accuracy of the CT model-method combined with static and dynamic radiostereometry is sufficient when examining large joints. However, for the method to be truly effective, an automated analysis method should be developed.
- The CT model-method could be the favorable method in future kinematic studies of large joints, since no implanted markers are needed.

**Strengths and limitations of this study:**

Eight donor legs were used for this study, and potentially the small sample size may lead to an overestimation of the accuracy.

- The following processes were automated, and the reproducibility of the processes was therefore not investigated.
  - CT-segmentation of the bone model.
  - Placing the anatomical coordinate system.
  - Detection and creation of the markers model.
- The comparison of the model-method and the marker-method was not blinded.

**1.INTRODUCTION**

To perform kinematic analysis of joints, an accurate and reliable method of tracking bone motion is needed (1). In radiostereometric analysis (RSA), tantalum markers are inserted into the bone during surgery to track the bones with stereo x-rays. This is currently widely used to monitor implant fixation and wear over time (2–4). RSA measurements have been shown to be very accurate and precise at the submillimeter level (2,5,6).

Dual-plane fluoroscopy using computed tomography (CT) bone-models have been used to record and calculate knee joint kinematics without markers (7–9). In 2003, a model-based RSA method was introduced allowing prosthesis tracking without the use of markers at the expense of a slight accuracy loss (10,11).

The accuracy of dynamic RSA using CT bone-models is expected to be similar to dynamic RSA using models of prostheses, which would be acceptable in studies examining movements of large joints. The

CT-bone-model-RSA method would be superior to skin marker based joint kinematics measurements that are exposed to soft tissue artefacts (1,12,13). Further, the model-method enables kinematic and stability comparison between pre-operative and post-operative, and injured and healthy joints without the need of inserting bone markers.

The purpose of this study was to evaluate the accuracy of the CT model-method for measuring knee joint kinematics with static and dynamic RSA using the marker-method as the gold standard.

## 2.MATERIAL AND METHODS

### *2.1 Specimens and dissection*

Eight paired fresh-frozen human (four female, four male) donor legs including foot, knee and hemipelvis were used for this study. Two of the donor knees had degenerative changes. The mean age of the specimens was 77 years.

### *2.2 Preparations for the RSA analysis*

A bead-insertion instrument (Kulkanon, Wennbergs Finmek, Sweden) was used to place eight to twelve 1 mm tantalum beads widely spread in the cortical bone of femur and tibia approximately five cm from the joint line through a 4 mm drill hole on the lateral side of the proximal tibia and the medial side of the distal femur.

### *2.3 CT bone-model*

The intact frozen leg specimens were scanned in a Phillips Brilliance 40 CT scanner using axial slices, 120 kVp, 150 mAs, slice thickness = 0.9mm, slice increment = 0.45mm, pixel size = 0.39mm×0.39mm.

The bone-models were constructed using an automatic graph-cut segmentation method (14,15). The method uses eigen analysis of the hessian matrix to identify the sheet-like structure of the bone surface and formulate a sheetness measure, which is subsequently used in a graph-cut optimization (16).

The reconstructed bone-models (figure a) included approximately 15cm of both the distal femur and proximal tibia. For each bone-model, a local coordinate system was created using a modified version of

the automatic method introduced by Miranda et al. (2010), where the diaphysis was fitted using a cylinder instead of the principal component analysis used by Miranda.

#### **2.4 Experimental setup and equipment:**

A custom build motorized fixture was built to support the thigh and lower leg while the area of the knee was kept completely free of materials to avoid image artefacts. The hemipelvis was fixed to the base of the apparatus using three regular screws in the sacrum, iliac crest and the pubic bone. The foot and ankle joint were fixed in a standard PRO+ FIXED WALKER (VQ OrthoCare, Irvine, USA). A stepper motor (NEMA 23, 3Nm, National Instruments) was installed along with pulley wheels, a timing belt and two linear slides to perform the controlled dynamic knee flexion motion from 0° to 60° of flexion and back at 0.1m/s. The recorded knee flexion angles were limited to be from 0° to 60° due to limitations in the size of the systems region of interest. Another NEMA 23 motor was mounted to the foot rest – making the internal rotation of the foot automatic at a speed of 0.001m/s. The slow speed enabled a manual stop of the motor when the desired torque was reached. The torque was measured using a torque sensor (TQ 201-500, OMEGA, USA) (accuracy =  $\pm 0.15\%$ , repeatability =  $\pm 0.03\%$ ) and an adjacent meter (DP25B-S-230, OMEGA, USA). Both motors were controlled using a driver (DM542A, Longs Motor, China) and a breakout board (DB25, Sunwin, China). Figure b shows the set-up.

#### **2.5 Radiographic setup**

The stereo radiographs were recorded using a dynamic RSA system (Adora RSAd, Nordisk Røntgen Teknik, Denmark). A sampling frequency of 10 frames/sec, a vertically placed calibration box with uniplanar detectors (Box 14; Medis Specials, Leiden, the Netherlands) and a vertical tube set-up ( $\pm 16$  degrees tube angle to horizontal) were used to maximize the visualization of the knee joint line during motion. The full detector size of 37 (horizontal) x 42cm was utilized for each detector to record the knee motion from 0° to 60° of knee flexion. The source image distance (SID) was 2.94m and the focus skin distance (FSD) was 2.4m, and were chosen to increase the region of interest. The exposure settings for static radiographs were; 70KV and 10mAs. For the dynamic radiographs it was; 90KV, 500mA, 2.5ms

roentgen pulse width and a synchronization delay between tubes of approx. 0.002ms (maximum allowed by the system = 0.1ms). The resolution of the static radiographs was 2208x 2688 pixels (0.16mm/pixel) and for the dynamic radiographs it was 1104x1344 pixels (0.32mm/pixel). The difference in resolution is due to limitations of the RSA system.

## **2.6 Test protocol**

Step 1; static stereo radiographs were recorded with the donor legs positioned in 0°, 30° and 60° of knee flexion measured with a goniometer. 4Nm of internal rotation torque was applied to the foot to simulate a loaded knee before recording. Step 2; dynamic RSA series (10 frames/sec) were recorded in two successive runs of motorized driven knee motion (~0.08 m/s) from 0° to 60° of knee flexion. 4Nm of internal rotatory torque was applied to the foot before recording, and the reached internal rotation angle was kept throughout the sequence, meaning that the applied internal torque varied during the recording. Step 3; the leg was repositioned, and step 1 and 2 was repeated. The specimens were simultaneously used in another study that assessed ligament stability in five situations, where the anterior cruciate ligament (ACL) and the anterolateral ligament (ALL) were successively cut and reconstructed and compared with the intact knee. A total of eight (legs) x three (flexion angles) x two (double examinations) x five (ligament situations) = 240 static radiographs were recorded.

From the dynamic series, radiographs were selected so they matched the static radiographs with knee flexion angles of 0°, 30° and 60° as determined by model position of tibia and femur during radiographic image analysis in ModelBasedRSA (MBRSA) and two ligament situations were used, resulting in eight x three x two x two = 96 dynamic radiographs.

## **2.7 Analysis of the radiographs**

Of the 240 planned static and 96 dynamic stereo radiographs, 228 static and 89 dynamic radiographs were used. Six static and three dynamic trials were not recorded by mistake, and in six static images and four dynamic trials, the fixture was positioned incorrectly. Of the 228 static radiographs, 139 (~ 3/5 of the 240 minus exclusions) were used to obtain a good alignment between the local coordinate systems of the



model-method and the marker-method. The remaining 2/5 ~ 89 (minus exclusions) static and dynamic radiographs were used to calculate the difference between the model-method and the marker-method. The static and dynamic radiographs were analyzed using the commercially available software; Model-Based RSA v.4.02 , RSAcore, Leiden. MBRSA automatically detects the bone contours and an operator needs to select the contours to be included in the pose estimation algorithm. The selected contours (figure c) for the femur were the shaft, the condyles and the articular surface, while for the tibia the shaft, the eminencies and the medial and lateral plateau were selected. The process of fitting the bone-models to the radiographs was done by two observers, who previously in a pilot study fitted 25 femur and tibia bone-models and together developed a consistent workflow to ensure that the same contours were used as much as possible.

The MBRSA software's three algorithms (17) were applied and used to estimate the pose of each CT-model by minimizing the matching error between the virtual projection of the bone-model and the detected projection (contours) in the radiograph.

The mean error of rigid body fitting is used to assess the mean error of marker detection between frames within a rigid body, and is recommended to be below 0.35mm (18). The mean condition number is used to assure an acceptable scatter of the injected markers, and is recommended to be below 120 in studies of the knee (18,19). The average mean error and the condition number for femur and tibia were calculated in 89 static and 89 dynamic radiographs.

## ***2.8 Inter- and intra-observer reliability measurements of the manual contour selection***

Inter- and intra-reliability measurements were performed of the manual contour selection and were completed by three observers. The observers (Obs.) were categorized as experienced (Obs. 1 with +500 RSA analysis), less experienced (Obs. 2 with +300 RSA analysis), and inexperienced (Obs. 3 with +50 RSA analysis). For both static and dynamic radiographs, three of the previously analyzed radiographs (0°, 30° and 60°) were used from each of the eight knees (n = 24). Each of the selected 24 static and 24

dynamic radiographs was reanalyzed two times (series 1 and series 2) with one week apart by all observers. The original image calibration and marker-model were kept intact in the radiographs, while the manual contour selection was redone, and therefore, the only possible difference in accuracy would be due to differences in the bone-models translation and rotation. After both analyses, the bone-models kinematic translation and rotation were extracted in all 6DOF.

## **2.9 Data analysis:**

The raw kinematic data from the MBRSA-analysis were extracted and processed in customly developed software (MATLAB R2015b, Mathworks, USA).

For the following two statistical comparisons of the marker-method and the model-method, a mixed model was used, taking into account the repeated measurements on cadaver, pair, knee flexion angle, ligament combination and repetitions. Model validation was performed by visually inspecting the residuals and fitted values. Wald tests were used to analyze the systematic difference using a 0.05 level of significance.

1) To compare the bones individually, we calculated the error in translation and the rotation between the marker-method and the model-method using the Pythagorean Theorem;  $e = \sqrt{x^2 + y^2 + z^2}$ , with  $x$ ,  $y$  and  $z$  being the error for either translations or rotations. Normally, the Pythagorean Theorem, cannot be used for rotations, but since the error in rotations is small, it is a good approximation (2). 2) The measured knee motion between the marker-method and the model-method was illustrated using Bland-Altman plots (20).

The mean error of rigid body fitting in femur and tibia was compared between static and dynamic radiographs using the Student's t-test.

For the intra-observer reliability measurements, the two image series from each observer were compared using Intra Class Correlation (ICC) and 95% confidence intervals. For the inter-observer reliability measurements, the three observers first analysis series ( $n = 24$ ) were compared using the ICC and 95% confidence intervals.

### 3. RESULTS

Figure d illustrates, for each leg, the error in translation and rotation between the model-method and the marker-method in both static and dynamic radiographs. The box to the far right marked “all” combines the errors of all legs, and Table 1, shows the statistical outcome of these combinations. The mean error in translation was maximal 0.62mm and for rotations maximal 0.96°. Femur had a significantly lower error compared to tibia in all examined groups except for translation in static radiographs. Comparing static and dynamic radiographs, the errors in the dynamic radiographs were only poorer for the tibia, while errors of the femur were not affected.

The mean differences between the model-method and marker-method of the 6DOF measured knee motion in the static and dynamic radiographs are shown in the Bland-Altman (BA) plots in Figure e. The BA plot for the static radiographs demonstrated a mean difference for all three rotations within  $-0.10 - 0.08^\circ$  and a Limit of Agreement (LoA) in the range  $\pm 0.76 - 1.26^\circ$ , while for the three translations, the mean was within  $-0.06 - 0.007\text{mm}$  LoA  $\pm 0.49 - 1.15\text{mm}$ . The dynamic radiographs showed a mean difference for the three rotations within  $-0.17 - 0.05^\circ$  LoA  $\pm 0.89 - 1.50$  and for the three translations the mean difference was within  $-0.23 - 0.16\text{mm}$  LoA  $\pm 0.75 - 1.34\text{mm}$ . The individual means and LoA's are presented in each subplot in Figure e. The differences in the means between the static and dynamic radiographs were small, while there was a tendency towards the dynamic radiographs having a larger LoA in all 6DOF. Visual inspections of the BA-plots for all 6DOF confirmed no concentration of observations and thereby no effect of either DOF or difference between intact and the knee with the ACL and ALL ligaments cut.

The roentgen systems post-processing software optimized continuously the image contrast of each radiograph during the dynamic sequences. Depending on the amount of the metal-fixtured visible in the radiograph, the image contrast changed, making the bone-model less visible. The highest amount of metal was included in 60 degrees of knee flexion. With reduced clarity of the bone-model, the edge detection during analysis was harder due to some “washed out” bone edges. The contrast changed also in the static

radiographs, but due to the high quality of these radiographs, we did not experience difficulties with edge detection.

The average mean error in rigid body fitting of femur in static and dynamic radiographs were 0.046mm and 0.060mm ( $p=0.003$ ) respectively, and for the tibia in static 0.071mm and dynamic 0.080mm ( $p=0.116$ ).

The mean condition number and standard deviation for femur were 29.5 ( $\pm 19.1$ ) and for tibia 29.8 ( $\pm 19.9$ ), indicating a good scatter of the markers.

The Intra-Class Correlation Coefficient (ICC [95% Confidence Interval]) for intra-observer reliability in the static radiographs were 0.98 [0.96;0.99] or better for all observers in all 6DOF. The ICC for inter-rater reliability for static radiographs were 0.99 [0.98;1.00] or better when comparing the kinematic results between all three observers in the 6DOF.

For the dynamic radiographs, the ICC for intra-observer reliability were 0.86 [0.68;0.94] or better for all observers. The ICC for inter-rater reliability among all observers were 0.95 [0.90;0.98] or better in the dynamic radiographs.

add a line in the results that a very experienced observer made a mistake of >5mm in 1 out of 24 analyses performing the automated contour detection. “

The mean difference between the model-method and marker-method of the 6DOF measured knee motion in the static and dynamic radiographs were compared between all observers. In six of the 18 comparisons of static radiographs, a significant difference in the mean was found. No significant difference of the mean was found in the 18 comparisons in dynamic radiographs between observers.

#### 4.DISCUSSION

This study evaluated the accuracy of the CT model-method for measuring knee joint kinematics in static and dynamic RSA using the marker-method as the gold standard. As expected, the results generated with the model-method differed from the marker-method.

The mean difference between the model-method and the marker-method (systematic error) of all 6DOF in the kinematic analysis of the knee joint was found to be 0.23mm/° or better for both dynamic and static radiographs. The random error in terms of 95% LoA was largest in both static RSA  $\sim \pm 1.3^\circ$  and dynamic RSA  $\sim \pm 1.5^\circ$  in internal/external tibial rotation. This is to be expected since the model-method is generally less accurate for rotation about the long axis due to the cylindrical shape of long bones. The second and third largest LoA in dynamic RSA was found in medial-lateral translation and varus-valgus rotation, respectively. These directions were out-of-plane, which previously have been reported to have a worse accuracy compared to in-plane motion (10). For the static RSA, the out-of-plane medial-lateral translation had the second largest LoA as expected, while the in-plane anterior-posterior tibial translation had a slightly larger LoA compared to the out-of-plane varus-valgus rotation.

The LoA of the three in-plane DOF in static radiographs were  $\sim \pm 0.8\text{mm}$  or better, while for the dynamic  $\sim \pm 1.1\text{mm}$  or better. The LoA was larger in all 6DOF when comparing the error of the dynamic to the static radiographs, which is similar to the results reported by Anderst et. al (7) when using biplane fluoroscopy and bone-models. Compared to that study (7), the present study found better or similar results for accuracy with dynamic RSA and bone-models, while for static RSA and bone-models our results were generally better for rotations, while generally worse for translations.

A comparison of the marker-method vs. model-method in dynamic and static radiographs (Table 1) for the two bones showed that the femur generally had a significantly lower mean total error compared to the tibia. This difference might be explained by the large size of the femoral condyles, opposite to the tibial plateau containing the eminencies, which are smaller bone parts and harder to locate on the radiographs. The result of the mean total difference between femur's marker-method and model-method did not differ when comparing dynamic and static radiographs as it did for tibia. A difference between static and dynamic radiographs was expected for both bones due to motion artifacts and the two times lower resolution in the dynamic radiographs.

For both the static and dynamic radiographs, the mean rigid body errors were within the limit of 0.35mm that are normally used in RSA analysis. The mean error of the markers was significantly higher for femur in the dynamic radiographs compared to the static radiographs, while it was not for tibia. This difference can have two causes: First; the lower resolution of the dynamic radiographs results in less accurate marker projection detection. Second; the motion artifacts of the bone moving in the dynamic radiographs results in less accurate marker projection detection. We expect the lower resolution having the largest influence as the leg moved very slow compared to the 2.5ms pulse width and the roentgen tubes were synchronized within 0.002ms with a maximum allowed time delay of 0.1ms.

A probable cause for the observed difference in error for the tibia between static and dynamic radiographs could be the anatomical shape of tibia's bone. The pose estimation of the tibia might have been worse, due to less good software recognition of especially the tibial plateau and eminencies when detecting edge contours. Further, the model-method was sensitive to image contrast changes, which inevitably occurred when the metal-fixtured moved into the image during knee flexion. This automatic contrast adjustment of the roentgen system might also have had a negative effect on the visibility of thin bone parts of the tibial plateau as compared to the thicker cortical bone of the femoral condyles.

The Bland-Altman plots confirmed no concentration of observations, which was possible, since the clarity of the bone-model was reduced with the metal-fixtured gradually moving into the image. Thus, the difference between the model-method and the marker-method could have been largest at 60°. Additionally, no concentration were found between the intact- and the knees with ACL and ALL ligament removed, confirming the model-method to be reliable in measurements of the knee joint with different ligament situations.

Both the intra- and inter-observer reliability measurements for the manual contour detection in static and dynamic radiographs were very good. These results are similar to the results found in a study using ModelBasedRSA to detect hip arthroplastic wear, where both the correlation in intra- and inter-observer reliability measurements were 0.997 or better in all cases (21).

However, in the present study, observer 2's calculated ICC for medial-lateral tibial translation in the dynamic radiographs was particular worse than the rest of the calculated ICC's, and was 0.86 [0.68 ;0.94]. The lower ICC score was caused by a mistake during analysis of one radiograph, which resulted in a translation error of -5.43 mm between tibias bone-model and marker-model. We did not reanalyze the radiograph, but it was detected as an outlier during the kinematic calculations, and could normally have been reanalyzed. By removing this single erroneous radiograph from the ICC calculation, the ICC increased from 0.86 [0.68 ;0.94] to 0.98 [0.95 ;0.99].

High correlations were expected in the present study, as the bone contours are detected automatically by the software and only have to be selected by the observer. As the contours are clickable, the "correct" contours are fairly easy to select, and we would expect lower correlations, if the observers were to draw the bone contours themselves instead of selecting them.

The mean kinematic difference between the marker-method and the model-method were calculated for the first series of analysis of each observer. These differences were calculated to investigate if one observer were significantly more accurate compared to the others. No observer was found to be better than the others regardless of their different experience level with model-based RSA.

It is not easy to compare our results to previously reported results. Most studies have either used biplane fluoroscopy and bone-models (7,22,23), RSA combined with models of metal prosthesis (10,24), or bone models (25), while to our knowledge, no accuracy studies have been reported using dynamic RSA and bone-models. Models of metal prosthesis have clear edges for contrast detection, while bones differ due to bone quality and comparisons between these methods are therefore not just. The accuracy results of the study by Seehaus (25) are worse than the results presented in the current study, which is most likely caused by cutting away the proximal tibia and distal femur for the placement of a knee prosthesis.

Knowledge of the accuracy and limitations of both the marker-method and the model-method will help us in the choice of the more appropriate method in future studies. The marker-method is still the gold

standard method (markers = submillimeter precision), but the advantage of the model-method is that pre-operatively measurements are also possible without implanted markers. Further, the bone-model offers a good non-invasive and alternative method for measurements of in-vivo knee kinematics, and no other similarly precise methods or tools are available. However, even though no implanted markers are needed, it is important to consider the additional required CT radiation dose with respect to the added benefit of a study before including patients. Further, researchers should be encouraged to perform relatively short dynamic experiments with live tissue involved.

In the future, we believe, the bone-model-method could be used for in-vivo studies of knee joint kinematics performed at a slow pace, and could potentially be developed further for clinical use as a diagnostic tool for assessment of ligament laxity. However, for the method to be truly effective an automated image analysis system with minimal necessary human interaction is required, since the time spend on manual analysis is prohibitive. In summary, this study found the mean error of CT bone-models combined with static RSA to be  $\sim -0.001^\circ$  with a maximum limit of agreement (LoA) in rotations of  $\pm 1.26^\circ$  or better, while for translations it was  $\sim -0.03\text{mm}$  LoA  $\pm 1.15\text{mm}$  or better. For the dynamic radiographs, the mean error for rotations was  $\sim -0.11^\circ \pm 1.50^\circ$  or better and  $\sim -0.04\text{mm}$  LoA  $\pm 1.34\text{mm}$  or better for translations. These results may encourage the use of bone-models and dynamic RSA for non-invasive kinematic knee joint analysis in the future. In conclusion, the CT model method combined with dynamic RSA may be an alternative to prior marker-based methods for kinematic analyses in a laboratory controlled setting.

## 5. REFERENCES

1. Benoit DL, Ramsey DK, Lamontagne M, Xu L, Wretenberg P, Renström P. Effect of skin movement artifact on knee kinematics during gait and cutting motions measured in vivo. *Gait Posture*. 2006 Oct;24(2):152–64.
2. Selvik G. Roentgen stereophotogrammetry. A method for the study of the kinematics of the skeletal system. *Acta Orthop Scand Suppl*. 1989 Jan;232:1–51.



- 416 3. Van Embden D, Stollenwerck G a. NL, Koster L a., Kaptein BL, Nelissen RGHH, Schipper IB.  
417 The stability of fixation of proximal femoral fractures: a radiostereometric analysis. *Bone Joint J.*  
418 2015;97-B(3):391–7.
- 419 4. Molt M, Toksvig-Larsen S. 2-Year Follow-Up Report on Micromotion of a Short Tibia Stem. *Acta*  
420 *Orthop.* 2015;86(5):594–8.
- 421 5. Kärrholm J. Roentgen stereophotogrammetry. Review of orthopedic applications. *Acta Orthop*  
422 *Scand.* 1989 Mar 30;60(4):491–503.
- 423 6. Bojan AJ, Bragdon C, Jönsson A, Ekholm C, Kärrholm J. Three-dimensional bone-implant  
424 movements in trochanteric hip fractures: Precision and accuracy of radiostereometric analysis in a  
425 phantom model. *J Orthop Res.* 2015;n/a – n/a.
- 426 7. Anderst W, Zauel R, Bishop J, Demps E, Tashman S. Validation of three-dimensional model-  
427 based tibio-femoral tracking during running. *Med Eng Phys.* 2009;31(1):10–6.
- 428 8. Tashman S, Anderst W. In-vivo measurement of dynamic joint motion using high speed biplane  
429 radiography and CT: application to canine ACL deficiency. *J Biomech Eng.* 2003;125(2):238–45.
- 430 9. Anderst WJ, Baillargeon E, Donaldson WF, Lee JY, Kang JD. Validation of a noninvasive  
431 technique to precisely measure in vivo three-dimensional cervical spine movement. *Spine (Phila*  
432 *Pa 1976).* 2011;36(6):E393–400.
- 433 10. Kaptein BL, Valstar ER, Stoel BC, Rozing PM, Reiber JHC. A new model-based RSA method  
434 validated using CAD models and models from reversed engineering. *J Biomech. Elsevier;* Jun  
435 1;36(6):873–82.
- 436 11. Valstar ER, De Jong FW, Vrooman H a., Rozing PM, Reiber JHC. Model-based Roentgen  
437 stereophotogrammetry of orthopaedic implants. *J Biomech. Elsevier;* 2001 Apr 30;34(6):715–22.
- 438 12. Stagni R, Fantozzi S, Cappello A, Leardini A. Quantification of soft tissue artefact in motion  
439 analysis by combining 3D fluoroscopy and stereophotogrammetry: a study on two subjects. *Clin*  
440 *Biomech.* 2005;20(3):320–9.
- 441 13. Garling EH, Kaptein BL, Mertens B, Barendregt W, Veeger HEJ, Nelissen RGHH, et al. Soft-  
442 tissue artefact assessment during step-up using fluoroscopy and skin-mounted markers (*Journal of*  
443 *Biomechanics* (2007) 40, SUPPL. 1, (S18-S24) DOI: 10.1016/j.jbiomech.2007.03.003). *J*  
444 *Biomech.* 2008;41(10):2332–3.
- 445 14. Krčah M, Székely G, Blanc R. Fully automatic and fast segmentation of the femur bone from 3D-  
446 CT images with no shape prior. *Proc - Int Symp Biomed Imaging.* 2011;2087–90.
- 447 15. De Raedt S, Mechlenburg I, Stilling M, Rømer L, Søballe K, de Bruijne M. Automated  
448 measurement of diagnostic angles for hip dysplasia. *SPIE Med Imaging, Int Soc Opt Photonics.*  
449 2013;867009–867009.
- 450 16. Boykov Y, Funka-Lea G. Graph cuts and efficient N-D image segmentation. *Int J Comput Vis.*  
451 2006;70(2):109–31.

17. Kaptein BL, Valstar ER, Stoel BC, Rozing PM, Reiber JHC. Evaluation of three pose estimation algorithms for model-based roentgen stereophotogrammetric analysis. *Proc Inst Mech Eng H*. 2004;218(4):231–8.
18. Valstar ER, Gill R, Ryd L, Flivik G, Börjén N, Kärrholm J. Guidelines for standardization of radiostereometry (RSA) of implants. *Acta Orthop*. 2005;76(4):563–72.
19. ISO 16087. ISO 16087:2013 Implants for surgery — Roentgen stereophotogrammetric analysis for the assessment of migration of orthopaedic implants. 2013;2013.
20. Bland JM, Altman DG. Measuring agreement in method comparison studies. *Stat Methods Med Res*. 1999;8(2):135–60.
21. Pineau V, Lebel B, Gouzy S, Dutheil JJ, Vielpeau C. Dual mobility hip arthroplasty wear measurement: Experimental accuracy assessment using radiostereometric analysis (RSA). *Orthop Traumatol Surg Res*. 2010;96(6):609–15.
22. Li G, Van de Velde SK, Bingham JT. Validation of a non-invasive fluoroscopic imaging technique for the measurement of dynamic knee joint motion. *J Biomech*. 2008 Jan;41(7):1616–22.
23. Tashman S, Bey MJ, Anderst W, Demps E, Zauel R. MODEL-BASED TRACKING OF KNEE KINEMATICS FROM BIPLANE RADIOGRAPHS: IN-VIVO VALIDATION. 52nd Annu Meet Orthop Res Soc. (Paper No: 0252).
24. Hirschler C, Seehaus F, Emmerich J, Kaptein BL, Windhagen H. Comparison of the Model-Based and Marker-Based Roentgen Stereophotogrammetry Methods in a Typical Clinical Setting. *J Arthroplasty*. Elsevier Inc.; 2009 Jun 1;24(4):594–606.
25. Seehaus F, Olender GD, Kaptein BL, Ostermeier S, Hirschler C. Markerless Roentgen Stereophotogrammetric Analysis for in vivo implant migration measurement using three dimensional surface models to represent bone. *J Biomech*. Elsevier; 2012;45(8):1540–5.

## 6.FIGURES AND TABLES:

Figure a – CT bone-model of the femur to the left and the tibia to the right with their local coordinate systems.

Figure b – Simple drawing of the setup.

Figure c – Left: Static radiographic image. Right: Dynamic radiographic image. The zoomed images show the resolution in the static image being two times higher compared to the dynamic image. The yellow and green circles indicate the fiducial and control markers in the calibration box. The dynamic radiograph is inverted compared to the static radiograph and is a standard setting of the RSA system, which was not changed prior to the recordings, however this difference poses no issues in analysis of the radiographs.

Figure d – The upper boxplot show the combined three-axis translation error and three-axis rotation error between the model-method and the marker-method in the static radiographs, whereas the lower boxplots illustrates the dynamic radiographs. Each box display the median, the 25th and 75th percentiles, while the whiskers extend to the most extreme points not considered outliers. Circles are outliers  $> \pm 2.7$  SD. Each bar (A-H) is a donor leg and the bar marked “all” is data from all the cadavers combined. A-B, C-D, E-F and G-H are paired legs from the same subject.

Figure e – The upper Bland-Altman plot show the CT bone-model compared to the marker-method of the static radiographs in all 6DOF, while the lower BA plot show data from the dynamic radiographs. Circles =  $0^\circ$ , Crosses =  $30^\circ$ , Squares =  $60^\circ$ . Blue observations = intact knee. Pink observations = with both the ACL and ALL ligaments cut. The p-value indicates if the mean is significant different from zero.

Table 1 – Mean error of the boxes marked “all” from figure 4. The p-value indicates the comparison of static and dynamic radiographs in the upper part of the table, while the total error of femur and tibia are compared in the lower part of the table.

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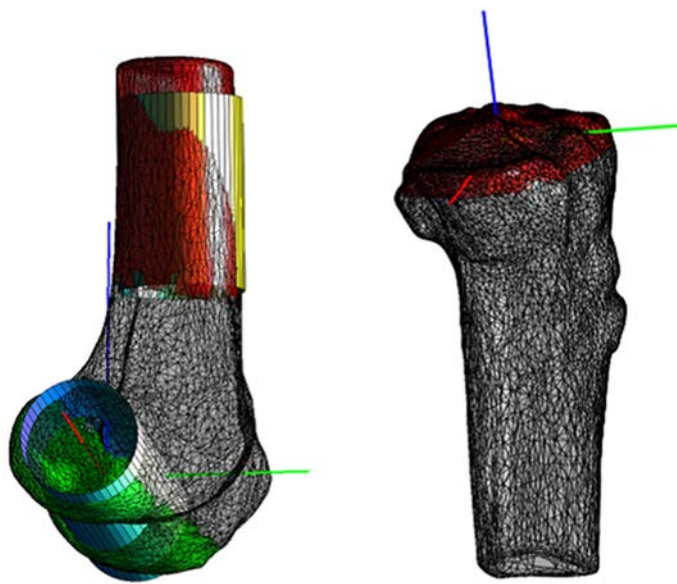
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### **Conflict of Interest Statement**

The authors of this paper have no financial or personal relationships with other people or organizations that could inappropriately influence (bias) our work, but it should be noted that Sepp De Raedt was employed at Nordisk Røntgen Teknik as a software developer during the study, and Bart L. Kaptein has been a part of the developing team of the software Model Based RSA.

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Figure a



**Figure b**

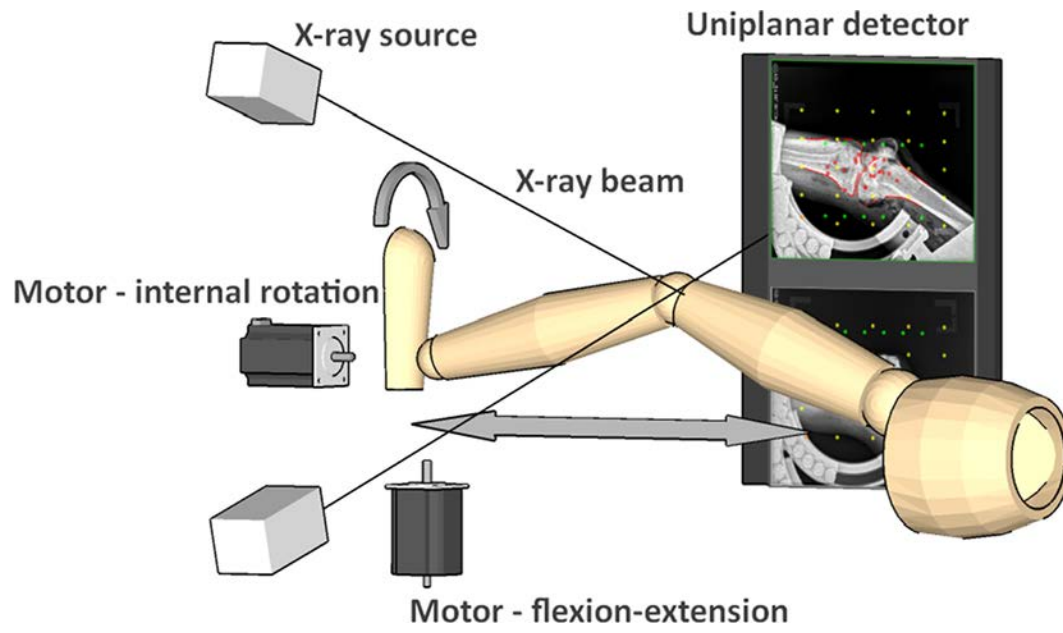


Figure c

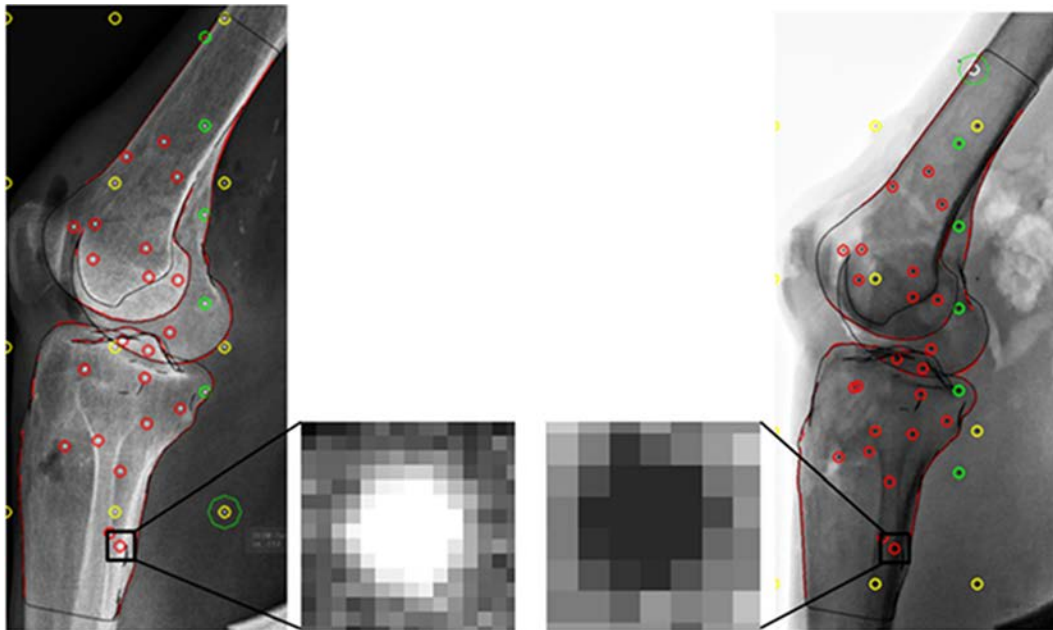


Figure d

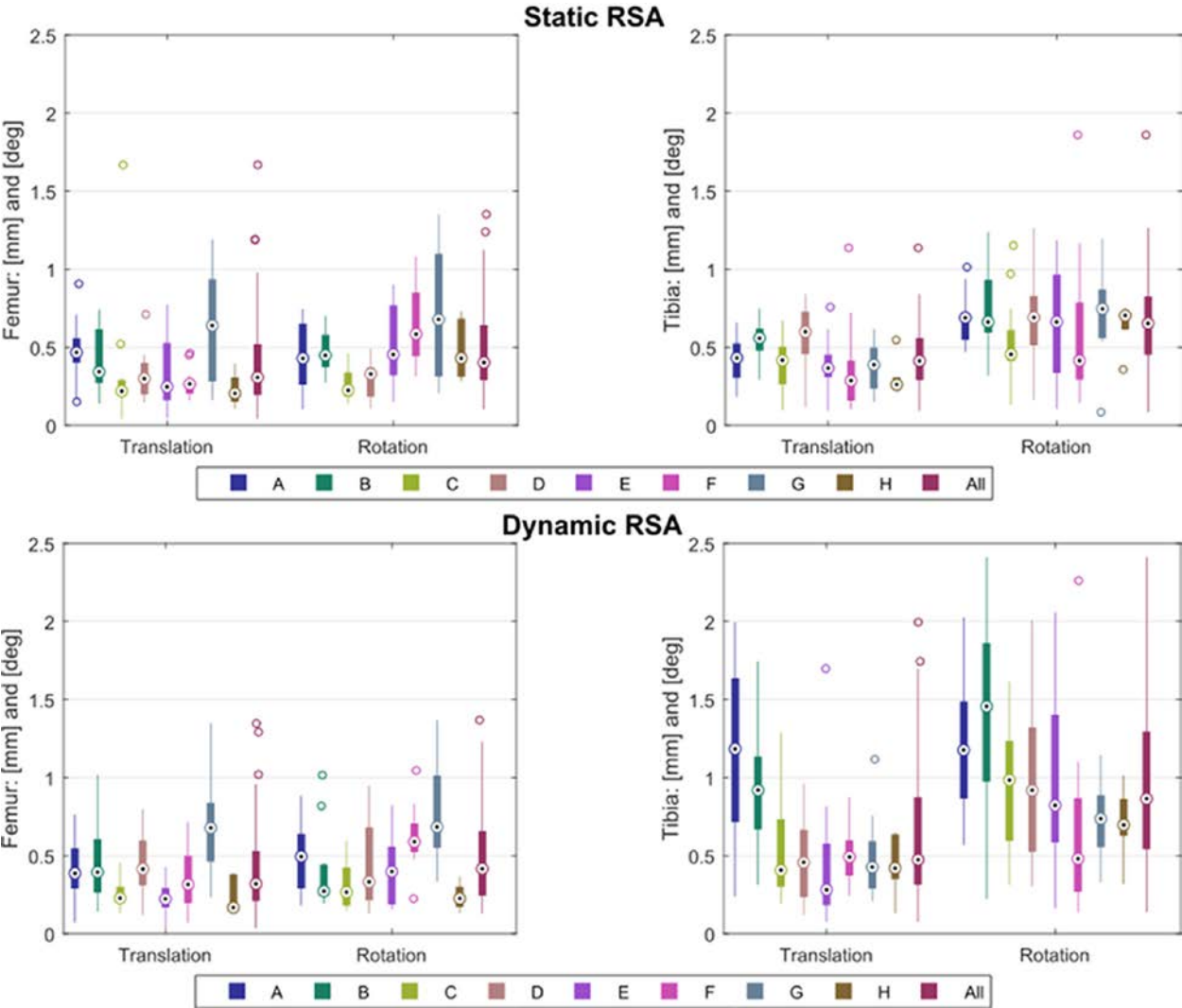
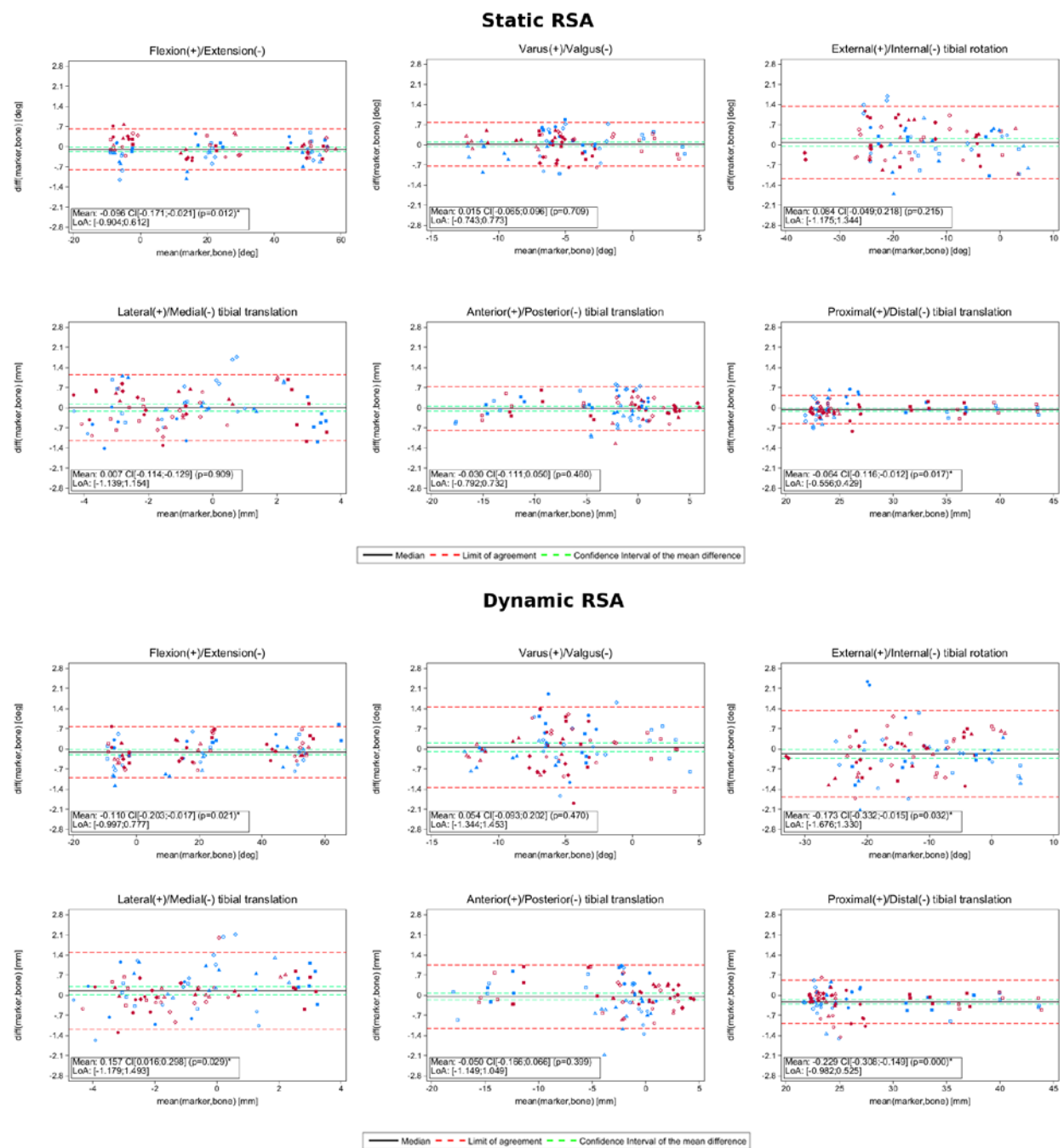




Figure e



**Tabel 1**

n = 89	Mean	CI	Mean	CI	P-value
	Static		Dynamic		
Femur – Translation [mm]	0.384	[0.284 ; 0.484]	0.391	[0.296 ; 0.487]	0.833
Femur – Rotation [deg]	0.477	[0.349 ; 0.605]	0.479	[0.389 ; 0.610]	0.948
Tibia – Translation [mm]	0.425	[0.344 ; 0.506]	0.619	[0.506 ; 0.733]	0.000
Tibia – Rotation [deg]	0.659	[0.571 ; 0.746]	0.960	[0.840 ; 1.081]	0.000
	Femur		Tibia		
Static – Translation [mm]	0.387	[0.317 ; 0.457]	0.429	[0.375 ; 0.482]	0.190
Static – Rotation [deg]	0.483	[0.358 ; 0.608]	0.665	[0.531 ; 0.799]	0.000
Dynamic – Translation [mm]	0.391	[0.291 ; 0.490]	0.620	[0.496 ; 0.743]	0.000
Dynamic – Rotation [deg]	0.469	[0.381 ; 0.557]	0.955	[0.823 ; 1.087]	0.000